

ASTRAZENECA PLC  
Form 6-K  
October 07, 2009

FORM 6-K

SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

Report of Foreign Issuer

Pursuant to Rule 13a-16 or 15d-16 of  
the Securities Exchange Act of 1934

For September 2009

Commission File Number: 001-11960

AstraZeneca PLC

15 Stanhope Gate, London W1K 1LN, England

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F  Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

Indicate by check mark whether the registrant by furnishing the information contained in this Form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes  No

If "Yes" is marked, indicate below the file number assigned to the Registrant in connection with Rule 12g3-2(b): 82-\_\_\_\_\_

AstraZeneca PLC

INDEX TO EXHIBITS

1. Press release entitled, “Phase III head to head trial showed ticagrelor reduced cardiovascular death and heart attacks over clopidogrel in acute coronary syndromes patients”, dated 1 September 2009.
  2. Press release entitled, “Transparency Directive Voting Rights and Capital”, dated 1 September 2009.
  3. Press release entitled, “Transaction by Persons Discharging Managerial Responsibilities Disclosure Rule DTR 3.1.4”, dated 1 September 2009.
  4. Press release entitled, “Publication of Prospectus”, dated 4 September 2009.
  5. Press release entitled, “Transaction by Persons Discharging Managerial Responsibilities Disclosure Rule DTR 3.1.4”, dated 8 September 2009.
  6. Press release entitled, “AstraZeneca and Nektar sign worldwide agreement for Nektar drug development programmes to address opioid-induced constipation”, dated 21 September 2009.
  7. Press release entitled, “US Court of Appeals affirms summary judgment decision in SEROQUEL patent litigation”, dated 28 September 2009.
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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

AstraZeneca PLC

Date: 2 October 2009

By: /s/ Adrian Kemp  
Name: Adrian Kemp  
Title: Company Secretary

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Item 1

PHASE III HEAD TO HEAD TRIAL SHOWED TICAGRELOR REDUCED  
CARDIOVASCULAR DEATH AND HEART ATTACKS OVER CLOPIDOGREL  
IN ACUTE CORONARY SYNDROMES PATIENTS

EFFICACY RESULTS ACHIEVED WITH NO INCREASE IN MAJOR BLEEDING

AstraZeneca today announced results from the phase III head to head trial, PLATO (A Study of Platelet Inhibition and Patient Outcomes), which demonstrate that ticagrelor (BRILINTA™) has achieved greater efficacy in the primary endpoint, reduction of cardiovascular events (CV death, MI, stroke) over clopidogrel (Plavix®/Iscover®) (9.8% vs. 11.7% at 12 months; 16% RRR; 95% CI, 0.77 to 0.92;  $p < 0.001$ ), without an increase in major bleeding (11.6% vs. 11.2%,  $p = 0.43$ ). This efficacy endpoint was driven by a statistically significant reduction in both CV death (4.0% vs. 5.1%,  $p = 0.001$ ) and heart attacks (myocardial infarction, MI) (5.8% vs. 6.9%,  $p = 0.005$ ) with no difference in stroke (1.5% vs. 1.3%,  $p = 0.22$ ). Ticagrelor is the first investigational antiplatelet that has demonstrated a reduction in CV death versus clopidogrel in patients with acute coronary syndromes (ACS). Primary results from the PLATO study were presented today at the European Society of Cardiology congress and simultaneously published in the New England Journal of Medicine (NEJM), [www.nejm.com](http://www.nejm.com).

For patients in the PLATO study, the reduction in risk of cardiovascular events with ticagrelor occurred early and this benefit increased over time compared to clopidogrel. Ticagrelor demonstrated a consistent positive effect across multiple secondary efficacy endpoints including CV death (and separately for all-cause mortality); myocardial infarction; the composite of myocardial infarction, stroke, and all-cause mortality. Among patients who received a stent during the study, a 33% reduction in risk of definite stent thrombosis was achieved with ticagrelor.

“The goal of new antiplatelet therapies is to improve the efficacy for patients without increasing the associated risks of treatment such as bleeding. Ticagrelor achieved a significant reduction in CV mortality in ACS patients versus clopidogrel and importantly without an increase in major bleeding,” commented Professor Lars Wallentin, co-chair of the PLATO Executive Committee, Uppsala Clinical Research Centre.

AstraZeneca Executive Vice-President Development, Anders Ekblom said, “The PLATO study was designed to reflect how patients with ACS are currently managed in clinical practice, by including patients who underwent invasive procedures and those who were managed with medication only. The PLATO data suggest ticagrelor could be a valuable new option for a broad range of acute coronary syndromes patients. We look forward to filing BRILINTA with regulatory authorities in the fourth quarter.”

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The PLATO study confirmed the clinical safety profile of previous ticagrelor studies which showed no difference in major bleeding compared to clopidogrel. When PLATO minor bleeding was added to the major bleeding results, ticagrelor showed an increase versus clopidogrel (16.1% vs. 14.6%,  $p=0.008$ ). There was also an increase in non-procedural related bleeding with ticagrelor. Within the patient subgroups of gender, weight, history of stroke/TIA, ticagrelor showed no increase in the incidence of major bleeding versus clopidogrel.

Consistent with phase II data, ventricular pauses (slowing of heart rhythms) occurred more often with ticagrelor but without associated symptoms or clinical consequences for the patient. Dyspnoea was reported more frequently by patients on ticagrelor (13.8% vs. 7.8%,  $p<0.001$ ) but did not represent new or worsening heart failure or lung disease. Only one in 100 ticagrelor patients overall stopped taking study medication due to dyspnoea.

PLATO analysed 66 subgroups (33 efficacy and 33 safety subgroups). Thirty of the 33 efficacy subgroups analysed were consistent with the analysis of efficacy in the overall population; showing a benefit for ticagrelor over clopidogrel. Of the three remaining subgroups, one (patients with weight below the gender-specific median) showed an attenuated benefit for ticagrelor over clopidogrel. The other two subgroups (patients not taking a statin medication on the day of randomisation and those at sites in North America) showed no treatment advantage for ticagrelor.

Of the 33 safety subgroups analysed, 32 were consistent with the analysis of safety in the overall population; showing no statistically significant difference between ticagrelor and clopidogrel. The remaining subgroup (patients with a Body Mass Index BMI  $>30\text{kg/m}^2$ ) had major bleeding more frequently with ticagrelor than with clopidogrel.

Given the large number of tests performed these differences may have been due to chance. The observed difference in results between patients in North America and those enrolled elsewhere raises questions of whether geographic differences between populations of patients or practice patterns influenced the effects of the randomised treatments, although no apparent explanations have been found to date.

“As a cardiology community, we are constantly seeking rigorously studied options to offer our patients who are facing an increased risk of serious, and potentially deadly, complications,” said Robert A. Harrington, M.D, co-chair of the PLATO Executive Committee, Duke Clinical Research Institute. “An estimated one in three ACS patients will die, have a recurrent heart attack or be readmitted to hospital within six months of their first cardiovascular event, so preventing reoccurrence is vital in ACS patient treatment.”

The PLATO results have confirmed AstraZeneca’s intention to submit the NDA and MAA with regulatory agencies during the fourth quarter of this year.

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PLATO was a head-to-head 18,624 patient outcomes study of ticagrelor plus aspirin versus the active comparator, clopidogrel plus aspirin, and was designed to establish whether ticagrelor could achieve meaningful cardiovascular and safety endpoints in ACS patients. Given the size of the PLATO database, we will continue to analyse and publish additional PLATO findings.

**NOTES TO EDITORS:**

Primary results from the PLATO study were presented today at the European Society of Cardiology annual meeting in Barcelona, Spain and simultaneously published in the online version of the New England Journal of Medicine (NEJM), [www.nejm.com](http://www.nejm.com).

**About BRILINTATM**

Ticagrelor (BRILINTA™) is an investigational oral antiplatelet treatment for ACS. BRILINTA (ticagrelor) is the first reversibly binding oral adenosine diphosphate (ADP) receptor antagonist. It selectively inhibits P2Y<sub>12</sub>, a key target receptor for ADP. ADP receptor blockade inhibits the action of platelets in the blood, reducing recurrent thrombotic events.

BRILINTA is the first in a new chemical class, the CPTPs (cyclo-pentyl-triazolo-pyrimidines) and is chemically distinct from the thienopyridines, such as clopidogrel and prasugrel.

AstraZeneca has proposed the name BRILINTATM. If approved by the FDA and the EMEA, it will serve as the trade name for ticagrelor. BRILINTA is a trademark of the AstraZeneca group of companies.

**About the PLATO study**

PLATO was an international head-to-head outcomes study of ticagrelor plus aspirin, versus clopidogrel plus aspirin. The PLATO study was designed to establish whether ticagrelor could achieve clinically meaningful cardiovascular and safety endpoints in ACS patients, above and beyond those afforded by clopidogrel, an irreversible therapy in the thienopyridine class of medicines.

The study design of PLATO was published in the April 2009 edition of the American Heart Journal.

**PLATO Bleeding Definitions:**

The bleeding definitions used within the PLATO trial were an evolution from the CURE bleeding definitions and were developed by the PLATO Executive Committee as constituting the most appropriate and clinically meaningful assessment of bleeding complications associated with acute and chronic therapy. The PLATO bleeding definitions provide a framework to allow investigators to record all bleeding events reported by patients in the PLATO trial. The bleeding definitions were developed to characterise bleeding in both the acute and long-term setting.

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PLATO Secondary Endpoints Results:

CV death (4.0% vs. 5.1%, p=0.001); Separately for all-cause mortality (4.5% vs. 5.9% with clopidogrel; p<0.001); myocardial infarction (5.8% vs. 6.9%, p=0.005); the composite of myocardial infarction, stroke, and all-cause mortality (10.2% vs. 12.3%, p<0.001); and a composite of cardiovascular death, myocardial infarction, stroke, transient ischemic attack, recurrent cardiac ischemia, severe recurrent cardiac ischemia, and other arterial thrombotic events (14.6% vs. 16.7%, p<0.001).

About AstraZeneca

AstraZeneca is a major international healthcare business engaged in the research, development, manufacturing and marketing of meaningful prescription medicines and supplier for healthcare services. AstraZeneca is one of the world's leading pharmaceutical companies with healthcare sales of US\$ 31.6 billion and is a leader in gastrointestinal, cardiovascular, neuroscience, respiratory, oncology and infectious disease medicines. For more information about AstraZeneca, please visit: [www.astrazeneca.com](http://www.astrazeneca.com).

CONTACTS:

Media Enquiries EU:

Sarah Lindgreen	+44 20 7304 5033	mob: +44 7827843832
Michele Pelkowski	+1 302 885 4055	mob: +1 610 812 3716
Chris Sampson	+44 20 7304 5130	

Media Enquiries US:

Emily Denney	+1 302 885 3451	mob: +1 302 897 4953
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Investor Enquiries UK:

Jonathan Hunt	+44 207 304 5087	mob: +44 7775704032
Karl Hard	+44 207 304 5322	mob: +44 7789654364

Investor Enquiries US:

Ed Seage	+1 302 886 4065	mob: +1 302 373 1361
Jorgen Winroth	+1 212 579 0506	mob: +1 917 612 4043

1 September 2009

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Item 2

Transparency Directive  
Voting Rights and Capital

The following notification is made in accordance with the UK Financial Services Authority Disclosure and Transparency Rule 5.6.1. On 31 August 2009 the issued share capital of AstraZeneca PLC with voting rights is 1,449,453,331 ordinary shares of US\$0.25. No shares are held in Treasury. Therefore, the total number of voting rights in AstraZeneca PLC is 1,449,453,331.

The above figure for the total number of voting rights may be used by shareholders as the denominator for the calculations by which they will determine if they are required to notify their interest in, or a change to their interest in, AstraZeneca PLC under the FSA's Disclosure and Transparency Rules.

A C N Kemp  
Company Secretary  
1 September 2009

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Item 3

Transaction by Persons Discharging Managerial Responsibilities  
Disclosure Rule DTR 3.1.4

We hereby inform you that on 31 August 2009, Michele Hooper, a Director of the Company, notified us that, on 31 August 2009, she purchased 1,200 AstraZeneca American Depositary Shares (ADSs) at a price of \$47.08 per share. One AstraZeneca ADS equals one AstraZeneca PLC Ordinary Share of USD0.25.

Following this purchase, Michele Hooper has a total interest in 1,700 shares, which represents approximately 0.0001% of the issued ordinary capital of the Company.

A C N Kemp  
Company Secretary  
1 September 2009

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Item 4

Publication of Prospectus

AstraZeneca PLC has published the attached prospectus dated 4 September 2009 in respect of its US\$5,000,000,000 Euro Medium Term Note Programme.

[http://www.rns-pdf.londonstockexchange.com/rns/5848Y\\_-2009-9-4.pdf](http://www.rns-pdf.londonstockexchange.com/rns/5848Y_-2009-9-4.pdf)

The Prospectus is available to the public for inspection at the following addresses:

Document Viewing Facility  
UK Listing Authority  
25 The North Colonnade  
Canary Wharf  
London E14 5HS

AstraZeneca PLC  
15 Stanhope Gate  
London W1K 1LN

A C N Kemp  
Company Secretary  
4 September 2009

Please note that the prospectus contains restrictions on the sale of the securities described therein to persons in certain jurisdictions and that the prospectus is not addressed to such persons, nor should such persons use or rely on the information contained therein.

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Item 5

Transaction by Person Discharging Managerial Responsibilities  
Disclosure Rules DTR 3.1.4R

We hereby inform you that the interest of Bruno Angelici, a person discharging managerial responsibility, in the shares of AstraZeneca PLC has changed as detailed below.

On 7 September 2009, Mr Angelici exercised an option over 37,728 AstraZeneca PLC Ordinary Shares at an option price of £22.31 per share. The option was granted to Mr Angelici in March 2003.

Following the exercise, Mr Angelici sold all of the 37,728 shares so acquired at a price of £27.95 per share.

A C N Kemp  
Company Secretary  
8 September 2009

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Item 6

**ASTRAZENECA AND NEKTAR SIGN WORLDWIDE AGREEMENT FOR NEKTAR DRUG DEVELOPMENT PROGRAMMES TO ADDRESS OPIOID-INDUCED CONSTIPATION**

AstraZeneca and Nektar Therapeutics announced today that they have entered into an exclusive worldwide license agreement for two drug development programmes: NKTR-118, a late stage investigational product being evaluated for the treatment of opioid-induced constipation, and the NKTR-119 programme, an early stage programme that is intended to deliver products for the treatment of pain without constipation side effects. Both programmes were developed by Nektar, utilizing their proprietary small molecule advanced polymer conjugate technology platform.

Under the terms of the agreement, AstraZeneca will assume the responsibility for the continued development of both the NKTR-118 and NKTR-119 programmes, including the initiation of late-stage clinical studies for NKTR-118. AstraZeneca expects completion of the design of the phase III programme in the near term, and anticipates filing the drug with regulators in 2013. AstraZeneca will also be responsible for global manufacturing and marketing for both programmes. Under the agreement, Nektar will receive an upfront payment of \$125 million for both NKTR-118 and NKTR-119.

NKTR-118 has completed a Phase 2 clinical trial and is being developed to treat constipation caused by the use of opioid pain products. Under the agreement, for NKTR-118, Nektar is eligible to receive up to \$235 million in aggregate payments upon the achievement of certain regulatory milestones, as well as additional tiered sales milestone payments of up to \$375 million if the product achieves considerable levels of commercial success. Nektar will also be eligible to receive significant double-digit royalty payments on net sales of NKTR-118 worldwide.

NKTR-119 is an early stage drug development programme that is intended to combine oral NKTR-118 with selected opioids, with the goal of treating pain without the side effect of constipation traditionally associated with opioid therapy. AstraZeneca will continue the development of this programme, including determining the appropriate opioid combinations with NKTR-118. For NKTR-119, Nektar would receive development milestone payments as well as tiered sales milestone payments. Nektar will also receive significant double-digit royalty payments on NKTR-119 net sales worldwide.

“NKTR-118 is an important late stage programme that has the potential to address a real need for patients,” said David Brennan, Chief Executive Officer of AstraZeneca. “We are excited about this agreement with Nektar, as it provides us the opportunity to apply our deep knowledge and expertise in neuroscience, oncology and gastrointestinal areas of medicine to create real value for patients. This is a good example of using externalisation to enrich the company’s late-stage pipeline.”

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“We are extremely pleased to enter into this exclusive global license agreement with AstraZeneca,” said Howard W. Robin, President and Chief Executive Officer of Nektar Therapeutics. “AstraZeneca has a strong history of creating and establishing market-leading brands, which makes them the ideal development and commercial partner for our NKTR-118 and NKTR-119 programmes. In addition to the promise that these potential products provide to patients, this partnership validates Nektar’s successful strategy to create novel oral small molecule drug candidates with our advanced polymer conjugate technology platform.”

NKTR-118 is an investigational drug candidate that combines Nektar's advanced small molecule polymer conjugate technology platform with naloxol, a derivative of the opioid-antagonist drug, naloxone. Results from NKTR-118’s Phase 2 clinical trial will be presented at an oral plenary session of the American College of Gastroenterology 2009 Annual Scientific Meeting in October.

The agreement is subject to review by the United States Government under the Hart-Scott Rodino Act and becomes effective after the expiration or earlier termination of the waiting period (or any extension thereof).

#### NOTES TO EDITORS:

##### About Opioid Induced Constipation

It is estimated that for those patients who take opiates chronically for pain management, anywhere from 40-90% of such patients will develop constipation. Less than half of those patients find effective relief from current treatment options that include prescription and over-the-counter laxatives and stool softeners. These symptoms of bowel dysfunction are a result of the drug binding to the mu-opioid receptor in the gut(1). Opioid-induced bowel dysfunction encompasses symptoms such as constipation, bloating, abdominal cramping, and gastroesophageal reflux. Constipation is the hallmark of this syndrome and is generally its most prominent component.

According to IMS Health, about 230 million prescriptions were written for opioids in 2007 in the United States alone. This is estimated to represent about 65-75% of the worldwide opioid market. Currently, there are no oral drugs approved that are indicated to treat opioid-induced constipation. Opioid bowel dysfunction and opioid-induced constipation can significantly impact quality of life and increase healthcare utilisation.

##### About Nektar

Nektar Therapeutics is a biopharmaceutical company developing novel therapeutics based on its PEGylation and advanced polymer conjugation technology platforms. Nektar's technology and drug development expertise have enabled nine approved products in the U.S. or Europe for partners, which include leading biopharmaceutical companies, including UCB's Cimzia®, Roche's PEGASYS® for hepatitis C and Amgen's Neulasta® for

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neutropenia. Nektar has created a robust pipeline of potentially high-value therapeutics to address unmet medical needs by leveraging and expanding its technology platforms to improve and enable molecules. Nektar is currently conducting clinical and preclinical programmes in oncology, pain and other therapeutic areas. NKTR-102, PEGylated irinotecan, is currently in Phase 2 clinical studies in ovarian, breast and colorectal cancer. NKTR-105, PEGylated docetaxel, is currently in a Phase 1 clinical study in patients with refractory solid tumors.

Nektar is headquartered in San Carlos, California, with additional R&D operations in Huntsville, Alabama and Hyderabad, India. Further information about the company and its drug development programmes and capabilities may be found online at <http://www.nektar.com>.

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#### Media Enquiries:

Chris Sampson	+44 207 304 5130 (24 hours)
Neil McCrae	+44 207 304 5045 (24 hours)
Sarah Lindgreen	+44 20 7304 5033 (24 hours)
Emily Denney (US)	+1 302 885 3451

#### Investor Enquiries UK:

Jonathan Hunt	+44 207 304 5087	mob:+44 7775 704032
Karl Hard	+44 207 304 5322	mob:+44 7789 654364

#### Investor Enquiries US:

Ed Seage	+1 302 886 4065	mob: +1 302 373 1361
Jorgen Winroth	+1 212 579 0506	mob: +1 917 612 4043

21 September 2009

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Item 7

US COURT OF APPEALS AFFIRMS SUMMARY JUDGMENT DECISION IN SEROQUEL PATENT LITIGATION

AstraZeneca today announced that the US Court of Appeals for the Federal Circuit has affirmed the Summary Judgment decision of No Inequitable Conduct in patent litigation involving SEROQUEL (quetiapine fumarate) tablets. In July 2008, AstraZeneca announced that the US District Court for the District of New Jersey granted the company's Motion for Summary Judgment of No Inequitable Conduct in litigation involving Teva Pharmaceutical Industries Ltd. and Sandoz, Inc.

This most recent decision, made public on 25 September 2009, upholds the District Court's judgment that Teva's and Sandoz's products will infringe AstraZeneca's SEROQUEL patent and that the patent is valid and enforceable. AstraZeneca had sued Teva Pharmaceutical Industries Ltd. and Sandoz, Inc. alleging infringement of AstraZeneca's patent as a result of Teva's and Sandoz's filings of Abbreviated New Drug Applications (ANDAs). Teva and Sandoz had conceded infringement and the validity of AstraZeneca's patent covering SEROQUEL. The ANDAs sought approval to market generic versions of SEROQUEL tablets in the US before SEROQUEL's patent expires. The patent covering SEROQUEL expires in September 2011, with paediatric exclusivity through March 2012.

Since the Federal Circuit Court of Appeals' affirmed Summary Judgment in favor of AstraZeneca, trial remains unnecessary.

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Media Enquiries:

Chris Sampson	+44 20 7304 5130 (24 hours)
Neil McCrae	+44 207 304 5045 (24 hours)
Sarah Lindgreen	+44 20 7304 5033 (24 hours)
Kirsten Evraire (US)	+ 1 302 885 0435

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Investor Enquiries UK:

Jonathan Hunt

+44 207 304 5087

mob:+44 7775 704032

Karl Hard

+44 207 304 5322

mob:+44 7789 654364

Investor Enquiries US:

Ed Seage

+1 302 886 4065

mob: +1 302 373 1361

Jorgen Winroth

+1 212 579 0506

mob: +1 917 612 4043

28 September 2009

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